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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20040122

Application Number: 08/942,369
Filing Date: October 02, 1997
Appellant(s): CHEN ET AL.

Richard San Pietro
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 6/6/2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that the group of claims 20-24, 26, and 31 and the group of claims 32-37 and the group of claims 38-43 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

4,046,138	LIBMAN et al.	9-1997
4,077,845	Johnson	03-1978

Brocco WO 94/16097. 7-1994.

ODAKA et al. JP 04051890 2-1992.

Thaller et al. Journal of Clinical Microbiology, volume 26, no. 4 (April 1988), pp. 791-793.

(10) Grounds of Rejection

Claims 20-24 and 31-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over JOHNSON (US 4,077,845) in view of LIBMAN *et al.* (US 4,046,138) and THALLER *et al.* (J. Clinical Microbiol. (4/1988), vol. 26 (4), pp. 791-793).

Claim 20 recites a method to simultaneously detect and determine the susceptibility of urinary pathogens to antimicrobial agents comprising (a) providing a multicompartment assay device with at least one compartment comprising a growth medium (capable of sustaining growth of total microbial organisms), at least one compartment comprising a uropathogenic specific medium (UTI medium) and at least one compartment comprising an antimicrobial susceptibility interpretation medium comprising an antimicrobial agent (interpretation medium), (b) placing a portion of the sample in each type of compartment, whereby metabolism of a signal generating substrate and production of a signal in the growth medium compartment indicates the presence of total microbial organisms, metabolism of a substrate and production of a signal in the UTI medium indicates the presence of uropathogens, and metabolism of a

substrate and detection of a signal in the interpretation medium indicates that the organisms lack susceptibility to the antimicrobial agent in the interpretation medium, and (c) examining the compartments to determine the presence of uropathogens in the samples and susceptibility thereof to antimicrobial agents. Claim 21 limits the sample to urine. Claim 22 limits the organisms detected to primary gram negative urinary pathogens. Claim 23 limits the pathogens of claim 22 to Enterobacteriacae. Claim 24 limits the pathogens of claim 22 to be selected from E. coli, Klebsiella spp., Enterobacter spp., Proteus mirabilis, Proteus vulgaris, Morganella morganii, Providencia retteri, and Acinobacter spp. Claim 31 limits a signal generating substrate to be fluorogenic or chromogenic. Claims 32-36 recite a method and limitations similar to those of claims 20-24, wherein claim 32 further limits the uropathogenic specific medium to comprise a methyl-umbelliferyl substrate, which when metabolized, indicates the presence of uropathogens in the sample.

JOHNSON teaches a process (method) for detecting and determining the susceptibility of specific microorganisms to antibiotics wherein a clinical (urine) sample is added to separate wells of a microtiter plate, which wells comprise a selective culture medium or blends of the selective culture medium and known antibiotics, the plate is cultured, then the wells examined for growth of microorganisms (col. 10, line 45-col. 12, line 2 and col. 7, lines 33-36). JOHNSON further teaches that his method and device may be used to analyze urinary pathogens, specifically *Escherichia coli*, *Klebsiella*, *Enterobacter*, and *Proteus* spp. (col. 3, lines 31-36). JOHNSON teaches that his sample may be urine, blood or spinal fluid, and that growth in individual growth wells

permits a positive test for indication of organisms (col. 7, lines 39-46). JOHNSON does not specifically teach a medium capable of sustaining growth of total microbial organisms nor a medium comprising a fluorogenic or chromogenic substrate.

LIBMAN teaches a device and method for detecting contaminating microorganisms (pathogens) in a urine sample wherein the sample is cultured on two or more different media, selective and nonselective (col. 3, lines 64-67). LIBMAN teaches that his nonselective media supports growth of urinary pathogens and contaminants.

THALLER teaches a selective, differential medium to screen for common gram-negative urinary tract pathogens (abstract), wherein the medium is inhibitory to growth of gram-positive organisms (p. 792, right column). THALLER teaches that metabolism of chromogenic and/or fluorogenic substrates, specifically a methyl-umbelliferyl-glucuronide, in her medium can produce detectable signals whereby urinary pathogens are detected (p. 792, left column and Table 1). THALLER specifically teaches that microorganisms detected using her medium include E. coli, Klebsiella species, an Enterobacter species, Proteus species, Morganella, and Providencia (Table 1). THALLER teaches that her medium provides several improvements over other selective media used in methods of detecting urinary pathogens (p. 792, right column).

It would have been obvious to one of ordinary skill in the art at the time of invention to include the nonselective medium of LIBMAN in the method of JOHNSON where the motivation would have been to provide a positive control for microorganismal growth, as suggested by JOHNSON. It would also have been obvious to use the selective medium of THALLER as the selective medium in the method of JOHNSON

where the motivation would have been to "analyze very selectively" for organisms causing an infection (JOHNSON, col. 3, lines 31-35) in order to presumptively identify the causative organisms in order to determine an appropriate course of treatment, as suggested by both LIBMAN (col. 2, lines 48-53) and JOHNSON (col. 3, lines 30-39). One would also have been motivated to use the selective medium of THALLER in the method of JOHNSON and LIBMAN because it is an improvement over other selective medium such as that taught by LIBMAN. One skilled in the art would reasonably have expected success in incorporating the selective and nonselective media of THALLER and LIBMAN in the method of JOHNSON because JOHNSON teaches sustenance of growth of total microbial organisms, which implies use of a nonselective medium, and because JOHNSON specifically teaches use of selective media. One skilled in the art would also have reasonably expected success in using the T-mod medium of THALLER as a selective medium in the method of JOHNSON because the THALLER specifically teaches that her medium is a selective, differential medium which may be used to successfully detect and identify gram-negative microorganisms in urine samples (p. 791), and specifically teaches that metabolism of a methyl-umbelliferyl substrate indicates the presence of E. coli, which are uropathogens.

Claims 38-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over JOHNSON (US 4,077,845) in view of LIBMAN *et al.* (US 4,046,138) and THALLER *et al.* (J. Clinical Microbiol. (4/1988), vol. 26 (4), pp. 791-793) as applied to claims 20-24 above, and further in view of ODAKA et al. (JP 04051890).

Claims 38-42 recite a method and limitations similar to those of claims 20-24, wherein claim 38 further limits the uropathogenic specific medium to comprise a yeast extract.

JOHNSON, LIBMAN, and THALLER make obvious a method of simultaneously detecting target microorganisms in a biological sample and determining susceptibility of the microorganisms to antimicrobial agents using a nonspecific medium and a medium specific for urinary gram negative pathogens, as set forth above. THALLER does not teach that her uropathogenic specific medium comprises yeast extract.

ODAKA teaches a culture medium to enhance growth and rapid detection of E. coli, a known uropathogen, and specifically teaches that methyl-umbelliferyl substrates can be detected in a medium comprising yeast extract (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to have added the yeast extract of ODAKA to the medium in the method of JOHNSON, LIBMAN, and THALLER where the motivation would have been to enhance growth of E. coli and allow for more rapid detection of uropathogens, as taught by ODAKA. One skilled in the art would reasonably have expected success in using a medium comprising the yeast extract of ODAKA to detect uropathogens (e.g. E. coli) in the method of JOHNSON, LIBMAN, and THALLER because both ODAKA and TAHLLER teach use of their media to differentially detect E. coli using methyl-umbelliferyl substrates.

Claims 26 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over JOHNSON (US 4,077,845) in view of LIBMAN *et al.* (US 4,046,138) and THALLER *et al.* (J. Clinical Microbiol. (4/1988), vol. 26 (4), pp. 791-793) as applied to claims 20 and 32 above, and further in view of BROCCO (WO 94/16097).

Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over JOHNSON (US 4,077,845) in view of LIBMAN *et al.* (US 4,046,138) , THALLER *et al.* (J. Clinical Microbiol. (4/1988), vol. 26 (4), pp. 791-793), and ODAKA et al. (JP 04051890) as applied to claim 40 above, and further in view of BROCCO (WO 94/16097).

Applicant claims methods of simultaneously detecting urinary pathogens in a biological sample and determining susceptibility of the pathogens to antimicrobial agents, as set forth above. Applicant further limits the antimicrobial agents to amoxicillin, clavulanic acid/amoxicillin, or enrofloxacin.

JOHNSON in view of LIBMAN and THALLER make obvious a method of simultaneously detecting target microorganisms in a biological sample and determining susceptibility of the microorganisms to antimicrobial agents using a nonspecific medium and a medium specific for urinary gram negative pathogens, as set forth above. JOHNSON in view of LIBMAN, THALLER, and ODAKA also make obvious a method of simultaneously detecting target microorganisms in a biological sample and determining susceptibility of the microorganisms to antimicrobial agents using a nonspecific medium and a medium specific for urinary gram negative pathogens, as set forth above. None of

JOHNSON, LIBMAN, THALLER, or ODAKA specifically teach amoxicillin, clavulanic acid/amoxicillin, or enrofloxacin.

BROCCO teaches a method of determining susceptibility of uropathogens, to amoxicillin and a clavulanic acid mixture (p. 5, line 8-p. 6, line 7 and p. 9, line 4-p. 10, line 15).

It would have been obvious at the time of invention to include the amoxicillin and clavulanic acid of BROCCO as antimicrobial agents in the method of JOHNSON in view of LIBMAN and THALLER or in the method of JOHNSOSN, LIBMAN, THALLER, and ODAKA where the motivation would have been to test susceptibility of microorganisms, specifically urinary pathogens/E. coli, to any known antibiotic or mixture of antibiotics, as suggested by JOHNSON, in order to determine an appropriate course of treatment for a subject infected with the microorganisms.

(11) Response to Argument

Section 1

In response to the argument that JOHNSON does not disclose "any medium whatsoever", it is noted that while JOGNSON does not specifically exemplify a medium, he does teach use of culture medium in his plates, and specifically teaches a selective medium and media which undergo an optical change as a result of metabolic action (growth) of microorganisms (col. 6, lines 48-60). The fact that the medium of JOHNSON is dried does not negate the fact that JOHNSON does, in fact, teach culture media, and particularly teaches use of selective media. It is noted that the rejections

are made under 35 USC 103, over a combination of references, wherein both LIBMAN and THALLER do exemplify culture media.

Appellant further argues that JOHNSON does not disclose use of his device for identifying organisms, for determining the presence of uropathogens, or for determining the antibiotic susceptibility of uropathogens. In response, it is noted that (a) the instant claims do not recite identification of organisms, but are directed to detection; and (b) JOHNSON specifically teaches, at column 3, lines 25-29 that his devices are "designed especially for conducting antibiotic susceptibility tests, i.e. tests to determine the effect of known antibiotics on microorganisms" and at column 3, lines 31-38 that "it is possible to analyze very selectively for ...organisms which account for the vast majority of pathogens found in urinary tract infections..." It is noted that the list of organisms disclosed by JOHNSON at column 3, lines 33-38 includes those recited in instant claims 24, 36, and 42.

In response to the argument that LIBMAN does not disclose "any original media", it is noted that the claims are not directed to an "original" medium, but recite a uropathogenic specific medium. Appellant admits on page 6 of the Brief that LIBMAN teaches a variety of media. It is again noted that the rejection is made over a combination of references wherein LIBMAN is relied upon for a teaching of a nonselective medium.

Appellant admits on page 6 of the Brief that the T-mod of THALLER is a medium for isolation and presumptive identification of Enterobacteriaceae, "many of which may be responsible for urinary tract infections". If a medium may be used to identify

organisms, then it necessarily is one which may be used for detection of those organisms. Appellant argues, however, that THALLER does not teach a uropathogen specific medium, "as defined in the application and recited in the claims". This argument is presented in more detail in Section 2 of the arguments.

Sections 2A and 2B

The examiner agrees that all limitations of a claim must be evaluated when determining obvious, as set forth on page 7 of the Brief, but also notes that limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The examiner also agrees that the specification, on page 12, defines a uropathogenic specific medium as one which allows only the growth of primary gram negative urinary pathogens and allows for substantially less growth of any other bacteria, and that at page 10, primary gram negative urinary pathogens are defined as those which cause 85-90% of all urinary tract infections, which pathogens include but are not limited to E. coli, Klebsiella spp., Enterobacter spp., and Proteus mirabilis. The examiner does not agree that the combination of references fail to make obvious the claimed method using a uropathogenic specific medium.

Appellant's arguments with respect to LIBMAN appear to agree that LIBMAN teaches a nonselective medium, or one which supports the growth of organisms and contaminants other than primary Gram-negative uropathogens. The claims specifically recite a medium "capable of sustaining growth of total microbial organisms"; i.e. a

nonselective medium. In view of this limitation, the medium of LIBMAN is not "outside the scope of the present claims", as argued on page 9 of the Brief. Appellant is reminded of his own argument on page 7 of the Brief that "all limitations" must be considered.

Sections 2B, 2C, 2D and 2E

The end of section 2B, the entirety of section 2C, and the beginning of section 2D appear to be directed to showing differences between various "prior art" media and that exemplified in the instant specification. It is noted that the medium used by applicants to generate the comparative data is not recited in the claims. Further, the "prior art" media tested is not the T-mod taught by THALLER and relied upon as the "uropathogenic specific medium" in the instant rejections. It is again noted that limitations from the specification are not read into the claims, as set forth above. The claims recite only a uropathogenic specific medium, which is defined as one which allows growth of primary gram negative urinary pathogens and allows for substantially less growth of any other bacteria.

The T-mod of THALLER is a "selective, differential plating medium to screen the common gram-negative urinary tract pathogens" as set forth on page 791. Further, THALLER specifically teaches that "gram-positive organisms were all inhibited on T-mode medium", thus, contrary to appellant's arguments, THALLER specifically teaches a medium which meets the definition of a uropathogenic specific medium. In response to the argument that THALLER does not disclose "identifying" organisms by their ability

to grow on the medium and provide a signal when a signal generating substrate is metabolized, it is again noted that the instant claim recite only detection, not identification. Further, as the T-mode of THALLER comprises a variety of signal-generating substrates, including a methylumbelliferyl substrate, as recited in the instant claims, and THALLER teaches that the presence of gram-negative urinary pathogens can be determined by detection of signals generated by metabolism (see Table 2), THALLER does teach a uropathogenic medium which meets the limitations of the instant claims.

Section 2F

In response to appellant's argument that ODAKA fails to disclose a uropathogenic specific medium, it is noted that ODAKA is merely relied upon for a teaching that yeast may be added to a medium to grow gram-negative organisms. The rejection is made over a combination of references wherein THALLER is relied upon for a teaching of a uropathogenic specific medium.

Sections 2G and 2H

In response to the argument that BROCCO does not "cure the failure" of the combination of JOHNSON, LIBMAN and THALLER, and does not disclose a medium specific for any organism, it is noted that BROCCO is relied upon for his teaching of specific antimicrobial agents which may be added to culture media. BROCCO is not relied upon for a teaching of a specific medium.

In response to the argument that the inventive medium may be used with a non-sterile sample, it appears that appellant is arguing that the inventive method produces unexpected results. In response, it is noted that the evidence presented in the Brief does not show unexpected results for a *claimed* medium over that of the T-mode of THALLER. In response to the argument that there is no motivation to combine BROCCO with the other references of record, it is noted that the rejection states , "the motivation [to combine] would have been to test susceptibility of microorganisms, specifically urinary pathogens/E. coli, to any known antibiotic or mixture of antibiotics, as suggested by JOHNSON, in order to determine an appropriate course of treatment for a subject infected with the microorganisms."

Section 3

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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January 22, 2004

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